JOURNAL OF CLINICAL RESEARCH BEST PRACTICES

Vol. 12, No. 2, February 2016 "Happy Trials to You"

Four Fundamental Issues An IRB Must Decide When Reviewing a Clinical Research Study

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Regulations and guidances lay out the ground rules for IRB review, but they do not provide a cookbook that an IRB can just follow when reviewing a clinical research study. Given that clinical research studies are *research*, important information about a study is often uncertain or simply unknown. An IRB must thus grapple with difficult questions that require sound judgment based on information that is seldom close to perfect. To approve a study, an IRB must conclude that the following four statements below are true:

1. The research question is scientifically important.

- What is the IRB's standard for "importance"?
- How important is the disease or medical condition being studied?
- Is the research question important because answering it will help better understand how the disease or medical condition can be better prevented, better diagnosed, or better treated?
- Is the research question important because answering it will shed insights into basic biochemical, genetic or mechanistic aspects of the disease or medical condition?
- Who measures importance, and how do they do it?
- To what extent has the research question already been answered by previous research?

2. The study has a sufficient probability of answering the research question.

- What probability of answering the research question does the IRB consider sufficient to justify approving the study?
- How does the IRB estimate the probability of success?
- What expertise does the IRB have among its members or outside experts to estimate the probability of success?
- What role does the study sponsor or principal investigator play in estimating the probability of success?
- How much credibility does the person or group making the estimate have?
- What does the IRB do if it does not have access to the necessary expertise?
- What evidence is there that the estimated chance of success is accurate?

3. The risk to study participants is acceptable, given the potential benefits to participants and the public.

- How does the IRB determine what constitutes an "acceptable level of risk"?
- How does the IRB accurately assess the individual and aggregate risks and benefits?
- What is an acceptable level of risk to the average participant in the research study?
- What is an acceptable level of risk to the participants most likely to be harmed in the research study?

- What risks and benefits do the study protocol and informed consent form specify?
- How significant are these risks and benefits, as measured by probability and severity/size?
- Does the study adequately minimize the risks and their potential impact?

4. The informed consent form clearly explains the required elements and other important information.

- Does the consent form address all the required elements and other important topics?
- How does the IRB determine whether the consent form will be understandable to a competent research subject?
- Does the IRB have a standard for competency and a tool for measuring it?
- How does the IRB ensure that only competent individuals give informed consent to study participation?

Authors

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